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NASOPHARYNGEAL PLASMABLASTIC LYMPHOMA: A CASE REPORT

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Plasmablastic lymphoma (PBL) is a rare aggressive subtype of non-Hodgkin's lymphoma (NHL). It occurs predominantly in older patients and HIV infected individuals and shows a predilection for the oral cavity. This case report describes a presentation of PBL in the nasopharynx of an older male patient. Due to its unusual immunophenotype and rare occurence it is often misdiagnosed by pathologists. The biggest challenge in the differential diagnosis of PBL is the distinction from plasmablastic (anaplastic) plasma cell myeloma, as the morphological and immunophenotypic features of these two entities overlap.

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Key words: *plasmablastic lymphoma, nasopharynx, immunohistochemistry*

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Introduction

Plasmablastic lymphoma (PBL) is a rare aggressive subtype of non-Hodgkin's lymphoma (NHL). Initially described in 1997, it occurs predominantly in older patients and HIV infected individuals and shows a predilection for the oral cavity.

Infection with Epstein-Barr virus (EBV) and human herpesvirus 8 (HHV8) has been proven in PBL tissue samples. Plasmablastic lymphoma has also been found outside the oral cavity, in the nasopharynx, lung, skin, various soft tissues, maxilarry sinus, intestines, heart (1). Although the majority of cases occur in immunodeficient patients, in a recent meta-analysis approximately 35% of cases occurred in immunocompetent individuals (2,3). The majority of patients reported were middle-aged men who were around 50 years old. However, the patients with HIV infection tend to have an earlier onset of the disease – they were around 38 years old. In rare cases, PBL is the initial presentation of HIV infection. The distribution of the disease in patients who have previously received organ transplants differs: lymph nodes and skin are the most common sites, with less frequent involvement of the oral cavity/jaw and gastrointestinal tract. Most cases of PBL present with advanced-stage disease (Ann Arbor stage III or IV) (4).

We present a case of plasmablastic lymphoma localised in the nasopharynx.

Patient

The 63-year-old male was referred from a general hospital outside Niš. He reported one sided nasal congestion and epistaxis for a period of few months. The patient's HIV status was unknown. During standard examination, endoscopy showed a pedunculated flesh-colored nasopharyngeal mass, 2 cm in its greatest diameter. The mass was surgically removed without any complications.

The surgically removed specimen was formallin fixed and paraffin embedded. Using standard procedures, H&E slides were made. After the initial microscopic examination without immunohistochemistry, the preliminary diagnosis was carcinoma sinonasalis dediferentiatum (anaplasticum). In order to confirm the diagnosis, the material was sent to the Center for Pathology and Pathological Anatomy, Clinical Center Niš, Serbia.

Immunohistochemistry was performed using the Dako Autostainer with Envision(+) Detection Kit at the Center of Pathology and Pathological Anatomy in Niš. Histologically, there were groups of densely packed oval and round shaped cells with scant reddish cytoplasm and eccentrically placed nucleus (Figure 1), with large areas of geographic necrosis. Some cells resembled plasmablasts. Determination of proliferative activity by immunohistochemistry was performed quantitetively by counting immunoreactive tumor cells in the most intensely stained areas in two high-power fields (x 400) by using ImageJ program cell counter, on 400 cells.

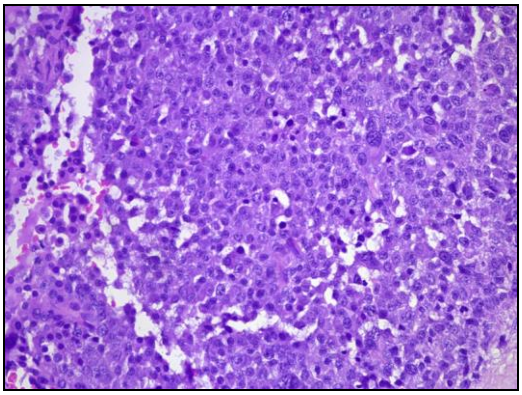

Figure 1. Nasopharyngeal tumor composed of oval and round shaped cells with eccentric nuclei and abundant eosinophilic cytoplasm, in a diffuse sheet-like and cohesive growth pattern. Apoptotic bodies and mitotic figures can also be seen. HE, Obj.x40

The Ki-67 index was defined as the percentage of immunoreactive tumor cells out of the total number of tumor cells. The Ki-67 index value was around 40% (Figure 2.A). Tumor cells were positive for CD138, CD38 (Figure 2.B), MUM-1 (Figure 2.C), lambda light chains positive (Figure 2.D) and negative for kappa light chains, CD56, EMA, LCA, cyclin D1, CD20, CD3, ALK, CD21, CD23 and CK5/6. Based on the morphological features and immunohistochemical profile, the diagnosis of plasmablastic lymphoma was made.

The patient was symptom-free at the time of this study, awaiting for his first treatment trial.

Discussion

Generally accepted treatment guidelines for plasmablastic lymphoma have not yet been established and treatment regimes largely vary and are usually a matter of physician discretion. The treatment consists mainly of chemotherapy, with the occasional use of radiotherapy (5).

Plasmablastic lymphoma is characterized by monomorphic cellular proliferation of round to oval-shaped cells with either centrally or eccentrically placed nuclei and abundant eosinophilic cytoplasm in a diffuse sheet-like and cohesive growth pattern, with large areas of geographic necrosis, and has two morphologic subtypes, monomorphic and plasmacytic.

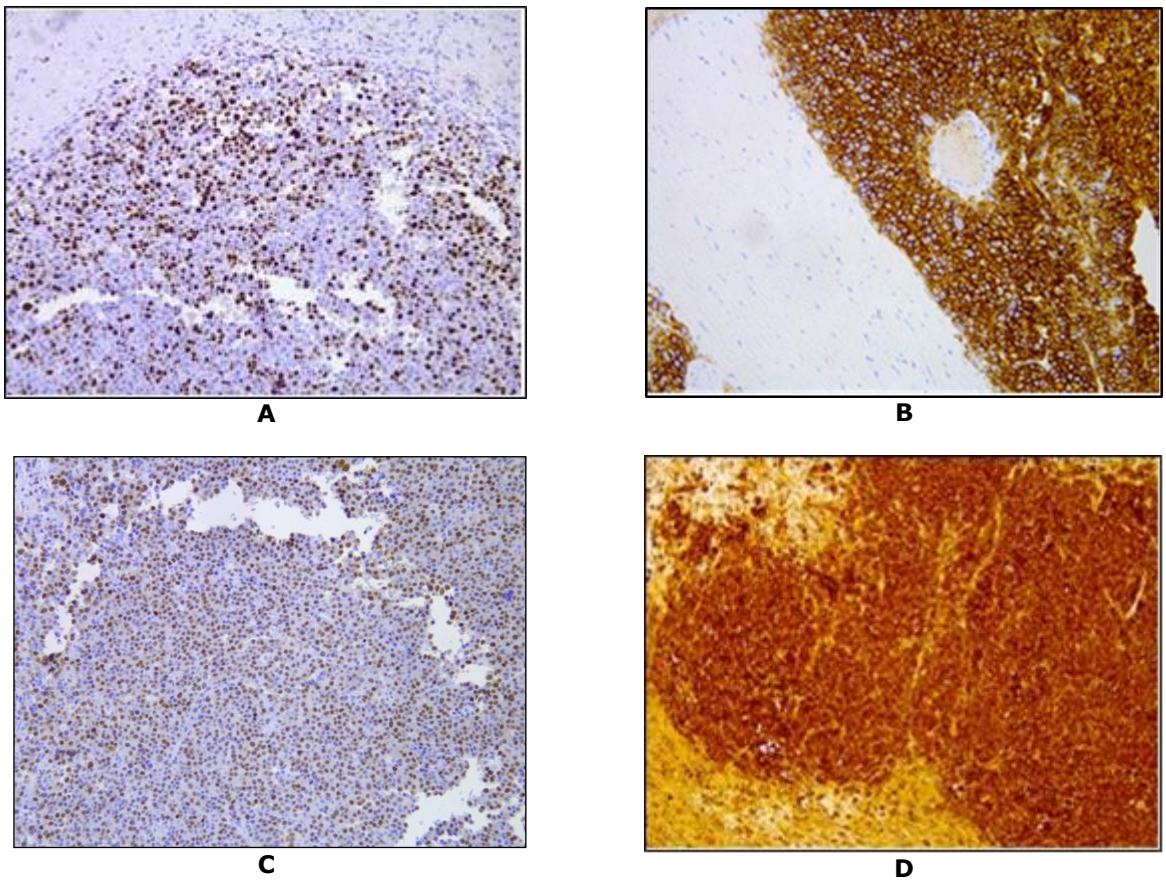

Figure 2. Immunohistochemical profile of nasopharyngeal tumor cells:
A) Ki-67 positive nuclei of tumor cells. Obj.x20.
B) CD38 positive tumor cells. Obj.x20.
C) MUM-1 positive nuclear stain. Obj.x20.
D) Neoplastic cells show intense positive lambda light chains staining. Obj. x20

Apoptotic bodies and mitotic figures are frequent, and tangible-body macrophages are easily detectable leading to a starry-sky appearance. PBL is a high-grade B-cell lymphoma that arises from post-germinal center B-cells and usually expresses the characteristic immunophenotype of plasmacytoid terminally differentiated B-cells. As plasmablasts acquire plasma-cell markers (i.e. VS38c, CD38, MUM1 /IRF4, CD138, EMA), they lose the leukocyte common antigen (CD45) and their B-cell markers CD20, CD79a, PAX5, and a high proliferation rate is reflected by Ki67 expression > 80%. Cytoplasmic immunoglobulins are expressed in near 70% of cases. Interestingly, these lymphomas might express epithelial and endothelial markers such EMA and CD31, respectively, posing some problems in differential diagnosis with poorly differentiated solid tumors. Recently, an immunohistochemistry staining for PRDM1 /BLIMP1 and XBP1 has been proposed to identify PBL (6).

The biggest challenge in the differential diagnosis of PBL is the distinction from plasmablastic (anaplastic) plasma cell myeloma, since the morphological and immunophenotypic features of these 2 entities overlap (7). A positive HIV status, EBV positive neoplastic cells, as well as high values of Ki67 proliferation index favor the diagnosis of PBL. On the other hand, clinical parameters and laboratory findings such as: renal dysfunction, a significant paraprotein, osteolytic lesions, hypercalcemia, and diffuse bone marrow involvement support the diagnosis of plasmablastic plasma cell myeloma (8). However, some cases occuring in HIV positive patients have overlapping features with plasma cell myelomas, such as lytic bone lesions and monoclonal serum immunoglobulins. In some cases a firm distinction cannot be made, and a descriptive diagnosis such as plasmablastic neoplasm, interdeterminate between plasmablastic lymphoma and anaplastic plasmacytoma may be acceptable. CD56 expression tends to occur more frequently in plasma cell neoplasms, but it also occurs in some PBLs and therefore cannot be used as a definitive criterion. In our case, tumor cells were CD56 negative. Cyclin D1 is negative in PBL but positive in a subgroup of patients with plasma cell myeloma. In our case, tumor cells were cyclin D1 negative.

Another important entity in the differential diagnosis of PBL is diffuse large B-cell lymphoma (DLBCL) with plasmacytoid differentiation, in which the absence of immunosuppression and lack of EBV infection are much more common than in PBL. Anaplastic lymphoma kinase (ALK) is an enzyme the expression of which defines a form of DLBCL that can often exhibit plasmablastic features. The presence of ALK expression by immunohistochemistry and identification of ALK gene rearrangement typically establish the diagnosis of ALK-positive DLBCL. Large B-cell lymphomas with plasmablastic features may occur as a rare transformation of small B-cell lymphoid neoplasms, mainly chronic lymphocitic leukemia and follicular lymphoma (9). Extracavitary/solid variant of primary effusion lymphoma (PEL) can closely resemble PBL, but these tumors are by definition positive for the HHV8 virus. Diffuse large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease is similarly positive for HHV8 by definition (10). In our case, tumor cells were ALK negative.

Lastly, we should also consider blastic plasmacytoid dendritic cell neoplasm (BPDCN) in the differential diagnosis of this tumor. Blastic plasmacytoid dendritic cell neoplasm is a clinically aggressive tumor, which frequently presents as cutaneous lesions and subsequently progresses to bone marrow (BM) involvement and leukemic dissemination (11). However, Dunlap et al. presented a case of BPDCN in the paranasal sinus. Immunophenotypic profile including a CD4+/CD56+/CD123+ population of cells in the absence of expression of B-cell (CD19, CD20, and CD79a), T-cell (CD3, cCD3, and CD5), or myelomonocytic (myeloperoxidase, lysozyme, CD14, and CD64) -specific antigens is needed for a diagnosis of BPDCN (12). In our case, tumor cells were CD21 and CD23 negative.

Conclusion

In our paper, a rare case of nasopharyngeal plasmablastic lymphoma was presented. Plasmablastic lymphoma is usually found in older patients and immunocompromised persons, with a predilection for oral cavity. Due to its unusual immunophenotype and rare occurence it is often misdiagnosed by pathologists. The biggest challenge in the differential diagnosis of PBL is its distinction from plasmablastic (anaplastic) plasma cell myeloma, as the morphologic and immunophenotypic features of these two entities overlap.

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Prikaz bolesnika

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NAZOFARINGEALNI PLAZMABLASTNI LIMFOM: PRIKAZ BOLESNIKA

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Plazmablastni limfom (PBL) je redak agresivni podtip nehočkinovog limfoma (NHL). Javlja se najčešće u usnoj duplji starijih bolesnika i HIV pozitivnih osoba. Prikazan je slučaj plazmablastnog limfoma u nazofarinksu starijeg muškarca. Zbog specifičnog imunofenotipa i retke incidencije ovog tumora česte su greške u postavljanju dijagnoze od strane patologa. Najveći izazov u diferencijalnoj dijagnozi plazmablastnog limfoma jeste njegovo razlikovanje od plazmoblastnog (anaplastičnog) plazmoćelijskog mijeloma, zbog morfoloških i imunofenotipskih osobina koje se preklapaju.

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Ključne reči: *plazmablastni limfom, nazofarinks, imunohistohemija*